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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/826,716	04/05/2001	Michael Karpusas	A062 US	4368

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EXAMINER

BORIN, MICHAEL L

ART UNIT PAPER NUMBER

1631

DATE MAILED: 12/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/826,716

Applicant(s)

KARPUSAS ET AL.

Examiner

Michael Borin

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 September 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 20 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 20 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 07/27/2004 has been entered.

Status of the claims

Claims 1-19, 21-33 are canceled.

Claim 20 is the only claim pending.

Claim Rejections - 35 USC § 112, second paragraph.

The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 20 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. The claim is amended to remove the objective of the claim. In its present version, the claim recites two method steps: performing fitting operation, and

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analyzing the data; however, it is not stated to which end these steps are performed.

B. The claim, step (a), addresses "experimental" employment of crystallographic coordinates. It is not clear how coordinates, which is a set of symbols, can be employed "experimentally" (as compared to "computationally", which is also recited by the claim).

C. It is not clear whether the term "homologs thereof" refer to "I domain of $\alpha 1$ chain of rat $\alpha 1\beta 1$ integrin", to "a complex $\alpha 1\beta 1$ integrin", or to either of them.

Claim Rejections - 35 USC § 112, first paragraph.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 20 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for using crystallographic coordinates of I-domain of $\alpha 1$ chain of rat $\alpha 1\beta 1$ integrin, does not reasonably provide enablement for using crystallographic coordinates of any complex or homolog thereof, or for using crystallographic coordinates of I-domains of $\alpha 1\beta 1$ integrins of other origins.

The specification indicates difficulties in obtaining crystals of I-domain of $\alpha 1$ chain of $\alpha 1\beta 1$ integrin, and specifies that all previous attempts of crystallizing has failed. See p. 20, lines 16-18. In the field of protein crystallography, it is well

established that the utilization of a variety of crystallization methods, for the protein in question, greatly improves the chances of identifying suitable conditions for crystallization. However, obtaining suitable single crystal(s) is the least understood step in the X-ray structural analysis of a proteins. Therefore, since the science of protein crystallization is underdeveloped, the crystallization of a protein is mainly a trial-and-error procedure. Further, it is well known that the homologous proteins from different sources cannot be easily crystallized using the same techniques and/or conditions and may result in different crystal forms. See, for example, Jan Drenth ("Principles of Protein X-ray Crystallography", pages 1-9).

While the skill in the art of crystallography is high, the science of protein structure and obtaining protein crystals is uncertain. Even utilizing the same source of protein and conditions for crystallization, a tiny variation in the way of receiving protein structure information and measurements can cause failure in obtaining useful results. Although, working examples are not, per se, required, the specification must provide an enabling disclosure for the invention as it is now claimed such that one of ordinary skill in the art could practice the invention without undue experimentation. It is noted that "only" the method of crystallizing of I-domain of $\alpha 1$ chain of rat $\alpha 1\beta 1$ integrin is prepared in the specification procedure and it would be undue experimentation to determine the crystallization conditions for other crystals for the reasons noted above.

Claim 20 is rejected under 35 U.S.C. 102(b) as anticipated by Qu et al (Proc. Natl. Acad. Sci., 92, 10277-10281, 1995; reference BD).

The claim is drawn to method comprising steps of employing crystallographic coordinates of I-domain of $\alpha 1$ chain of $\alpha 1\beta 1$ integrin, or a complex of $\alpha 1\beta 1$ integrin, or homolog thereof in a "fitting operation" with a chemical entity, and I-domain of $\alpha 1$ chain of $\alpha 1\beta 1$ integrin, or a complex of $\alpha 1\beta 1$ integrin, or homolog thereof.

Qu et al describe crystal structure of the I domain of complex of CD11a (i.e., of an $\alpha 1\beta 1$ integrin). The reference utilizes crystallographic coordinates of the I-domain to address interaction of the I-domain and Mn^{2+} ion (viewed as a "chemical entity") and discusses association of Mn^{2+} with various part of the I-domain,. See p. 10279. As such, the reference teaches the steps of fitting and analyzing of the instant method.

Claim 20 is rejected under 35 U.S.C. 102(b) as anticipated by Lee et al or Mayo et al (US 2003005440; priority date 07/10/2000).

Similarly to Qu et al, Lee et al or Mayo et al describe crystal structure of the I domain of MAC-1 (see Lee, abstract, Mayo, claims 29,30, section "Computational Design"). MAC-1 is an integrin from macrophages which has α subunit different

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from $\alpha 1\beta 1$, but quite similar structurally (see Mayo, paragraph [0009]. Therefore, the references teaching complex of crystals of I-domain of MAC-1 read on "homologs" of I-domain addressed in the instant claim. The references teach utilizing crystallographic coordinates of the I-domain to address interaction of the I-domain and metals and ligands. See Lee et al., abstract. See Mayo, paragraphs beginning from paragraph #[0317].

Claim 20 is rejected under 35 U.S.C. 103(a) as being obvious over Qu et al. The reference is applied as discussed above. Further, the reference teaches that I-domain contains binding sites for such physiological ligands as ICAM-1 and ICAM-3 (p. 10279, left column, bottom). Although the reference does not perform direct "fitting operations" with ligands other than Mn^{2+} , it would be *prima facie* obvious to one skilled in the art at the time the invention was made to employ the structural coordinates of crystal of I-domain obtained by Qu to identify interaction of $\alpha 1\beta 1$ integrin with its ligands, such as ICAMs.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Borin whose telephone number is (571) 272-0713. The examiner can normally be reached on 9am-5pm.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571) 272-0722. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michael Borin, Ph.D.
Primary Examiner
Art Unit 1631



11/25/04